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Transcript – Lecture 8

So we're going to continue our discussion about genetics and patterns of inheritance. We're going to go relatively quickly compared to last time. We've got a lot to get through today so I'm going to go relatively quickly.

And I printed a handout for you because I'm going to rely on the PowerPoint to a greater degree than I have before. So I want you to have them in case you want to take notes on them. OK? And we will do that occasionally for particular lectures. Now, importantly, we teach you about inheritance, not so much because we think you need to know about peas but rather the rules of inheritance which were derived from such studies but applied to many other studies.

Including in agricultural settings, in research settings in the laboratory involving fruit flies and mice, but more relevant to you to humans. The rules that Mendel laid down apply to you and allow us to predict inheritance patterns based on visible traits but also disease traits. And you'll see in next lecture that the information that we've given you helps us understand inheritance of various forms of genetic disease and predict, for example, frequencies within such pedigrees.

OK. So, firstly, I wanted to review some terms which you need to know. And I'll use a lot today. The genotype which is the alleles present for a given gene in an individual. OK? The genes. The alleles. The term homozygous which means having two of the same alleles.

Heterozygous, having two different alleles for a given gene. The phenotype which refers to the trait. That's what the researcher or the individual observes. The manifestation of the activity of those genes, of those alleles, the observed trait. The first filial, or F1, generation which is the product of a cross of individuals who are homozygous for different alleles of a given trait.

I think this should say gene, not given, given. Such that the F1 individual is heterozygous for that gene. That is, has two different alleles. If you cross two F1s together you generate the F2 generation.

The products of an F1 intercross. And based on Mendel's First Laws, which I told you about last time and I'll reiterate in a second, the ratio of the genotypes that you see in the F2 generation is 1:2:1.

Homozygous for one allele, heterozygous and homozygous for the other allele; 1:2:1. And the ratio of phenotypes is 3:1. That assumes that there is a simple dominant recessive relationship between the two alleles. We closed with that last time. The dominant is the allele that determines the phenotype in a heterozygous individual. Big S, little S you're smooth. Big S is dominant over little S.

Recessive allele is the opposite. In a heterozygote it's not seen. And, in fact, the only time you see the phenotype associated with the recessive allele is when the organism is homozygous for that recessive allele. And finally there's a term codominance, which I'm going to mention now. They don't really need to know, Claudette? We bring it up in Section, so I'm going to mention it here. And I refer you to the relevant parts of the book, but I'm not going to cover it in lecture but I'll show you where to go in the book to review that.

And that's relevant because Mendel's Rules apply as simple dominant recessive relationships, but they actually don't apply in terms of scoring them when you have a codominant situation. So this is Mendel's First Law laid out for you. When any individual produces gametes, germ cells, sperm, egg, the alleles, for a particular gene which control particular traits separates, so that each gamete receives only one of a pair of alleles present in the original individual.

And, as I said just a second ago, these experimental tests work well when there's a simple dominant recessive relationship between those two alleles. There are exceptions to this in terms of codominance and incomplete dominance. And I refer you to Figures 10.13 and 10.14 in your book which show you examples from fruit flies as well as, sorry, from humans as well as from pea plants that illustrate both codominance and incomplete dominance.

Now, to emphasize the simplicity, really, of Mendel's First Law, I want to show you an example which also derives from your book using coins. OK? And it's just to emphasize the point about probability. So what this says is that you have two, if you have two alleles of a given gene, big A, little A, big S, little S, you're going to hand off to your germ cells one or the other with equal probability.

And your mate will do the same such that the genotype of the offspring is the product of the probabilities of the genotype of the germ cells. OK? So I have two coins here, two pennies which have a head and a tail. All right? Head. Tail. So if I flipped this coin, what's the likelihood that this is a head? 1:2. If I flip this coin, what's the likelihood that it's a head?

1:2. If I put these together, like in fertilization, what's the likelihood that it's both heads? 1:4. Very good. One in two times one in two is one in four. That's really the essence of Mendel's First Law that the alleles segregate randomly into the germ cells, and you can then figure out Punnett Squares and the phenotype based on the probabilities of the different genotypes that derive from that simple calculation.

OK. We'll come back to a slightly more complicated version momentarily. OK. Now, last time we talked about smooth and wrinkled peas. I don't like this yellow chalk. Is there white chalk here?

We talked about smooth and yellow peas, smooth and wrinkled peas. We talked about genotypes, big S, big S, big S, little S, little S, little S. Remember that? We talked about phenotypes. What's the phenotype of this pea? Smooth.

What's the phenotype of this pea? Smooth, because you know that big S is dominant over little S. And what's the phenotype of this pea? Wrinkled. Good. What if I gave you, I handed to you on your dinner plate a smooth pea?

What's its genotype? What's its genotype? Who wants to venture out into the unknown here? What's its genotype? Come on. Yes? Thank you. You don't know what its genotype is because it could either be big S, big S or big S, little S.

It could either be big S, big S or big S, little S. How are you going to tell? How can you tell? You can test it. You could do what we call a Test Cross with a tester strain. And a tester strain is homozygous for the recessive allele.

OK? And based on this test we can figure out whether we're dealing with a big S, big S or big S, little S pea. So we're going to do this using Punnett Squares to emphasize the use of Punnett Squares. We have two possibilities.

Either our pea is big S, big S or our pea is big S, little S. Either way we're going to cross it to a pea, really a pea plant, but a pea that's little S, little S. OK? Now, when I generate a Punnett Square what gametes do I put over here? What alleles do I put over here?

Little S, little S. This plant only gives the little S allele to its gametes because that's all it has. What alleles do I put over here? Big S on both because this plant only gives big S to its gametes. And so therefore all of the offspring will be heterozygous, big S, little S, big S, little S. And what will the phenotype be of all of the offspring?

Smooth. 100% smooth. OK. And how about over here? Well, this side of the Punnett Square is the same. This individual only gives little S to its gametes. And how about over here? Flip a coin, half of the time it's big S, half of the time it's little S.

If this gamete meets up with this one then that individual is going to be big S, little S. The same thing over here. With this gives little S, little S, this is the same thing. What are the phenotypes here? Half and half. 50% smooth, 50% wrinkled.

OK. That's great. Now --

What I want to now consider is a second trait. And after we do this we're going to consider the inheritance of the two traits together, but let's just introduce the second trait now.

The gene is the Y gene. There are, again, two alleles, big Y and little Y. And the phenotypes associated with these genotypes are yellow and green. OK?

Mendel does a lot of crossing, etc., creates pure breeding strains, the parental strains. And I'm going to tell you that their genotypes are homozygous big Y, and these produce yellow peas. He also produces pure breeding strains that only ever produced green peas, and their genotype is little Y, little Y.

You cross these together to generate the F1. What's the genotype with respect to Y in the F1? Big Y, little Y. They're all big Y, little Y. And what's the phenotype of the F1? You don't know. That's very good, because I haven't told you which is dominant over which. By convention, you might have guessed that big Y was dominant over

little Y. And if that were true, and it is, then what would be the phenotype?

Yellow. And from that you can conclude that Y is dominant over little Y. OK? I always run out of space. Do these boards get smaller every year? I mean it's unbelievable to me.

Now, if we take these F1s and do an intercross to generate F2s, we're just reinforcing things we just learned here, in the F2 generation we're going to generate individuals who are Y, Y, big Y, big Y, big Y, little Y and little Y, little Y. What will be the frequency of generating such individuals in this cross?

One quarter will be like this, a half will be like this, a quarter will be like this, and that would give a ratio of 1:2:1. The phenotypes associated with that will be yellow, yellow and green.

So the ratio of the phenotypes will be 3:1. OK? We just redid Mendel's First Law for you. Now, what happens when we consider the two of these traits together, smoothness and color in the same cross? Well, this led Mendel to propose his Second Law which is illustrated here, which is that alleles of different genes, the S gene and the Y gene, assort independently of one another in producing gametes.

What happens for one does not effect what happens to the other. And this is true for genes that lie on separate chromosomes. Although it's not necessarily true for genes that lie on the same chromosome. I make that point here, and I'll make it again later because I don't want you to come to the conclusion that two genes always assort from one another independently. They do, and Mendel's Second Law is based on that, in some instances, but they don't always.

So to illustrate that point we turn to the coins again. I always also lose the coins. OK. So now we have our pennies once again, heads and tails. And dimes, heads and tails, yeah? OK. So I'm going to put a penny and a dime in each pocket. What's the frequency of generating a penny in the head configuration and a dime in the head configuration together?

Well, let's do it differently. What's the frequency of generating a head, a penny in the head configuration here? 1:2. What's the frequency of getting a penny in the head and dime in the head? One over four. It's one in two times one in two. And what's the frequency of getting penny head, dime head in this hand? One over four.

So what's the frequency of getting penny head, penny head, dime head, dime head in the zygote? 1:16. Again, simple probabilities. OK? And for Mendel's Second Law in its simplest form, it determines what you would expect to see in such crosses. And, again, we'll come back to a twist on that in a moment. Now, in biological terms it looks like this. And this derives from your book, so you can go and look at it.

It's adapted from Purves 10.8. And there's a nice little animation that goes along with that. But we're going to go through this because there's some subtlety here that I want you to understand. So here is the parent. It's a diploid. It has the two chromosomes that are relevant that carry the S gene and the Y gene. And the parent is heterozygous for both. It's a double heterozygote. Big S, little S, big Y, little Y. OK?

Now, when this individual undergoes meiosis, it can generate four possible haploid gametes. And those have the genotypes of all four combinations. It can be big S, little Y, big S, big Y, little S, little Y, little S, big Y. All four possibilities. And based on the simple laws of probability that we just went through with the coins, those are generated in equal amounts amongst the gametes.

OK? They're generated in equal amounts amongst the gametes. Why are they? Well, let me just show you another slide that illustrates it in slightly more detail. When these guys undergo the first, undergo duplication to generate the two chromatids for each chromosome, enter prophase of meiosis one, the homologs pair, as you recall.

The two chromosomes don't have anything to do with one another. The homologs pair but the two chromosomes don't have anything to do with one another. They're independent of each other. Now, if we consider this chromosome, the one that carries the S gene, it will line up on the metaphase plate in an orientation which is random. In this particular example, the big S allele is pointing down and the little S allele is pointing up. OK?

Based on that, let's fix that. Based on that there is one of two possible alignments for the chromosome that carries the other gene. In our example it's the Y gene. One orientation would have the big Y carrying chromosome pointing up, but it's just as likely that that chromosome could end up the other way around such that the big Y carrying chromosome is pointing down.

And it's based on the fact that the two chromosomes are independent of one another when they choose which side of the metaphase plate to go to that gives us this random assortment in meiosis and the development of Mendel's Second Law. So if you carry this through then you generate these gametes in a 2:2:2:2 or 1:1:1:1 ratio. OK? That's the most important thing. If you understand that then you can work it out as to which genotypes you get and which phenotypes you get using Punnett Squares.

OK? But it's important that you understand why it is that you get random assortment of the alleles in such a cross. Is that clear to everybody? It's probably not clear to the guy reading the newspaper. Oh, the woman reading the newspaper. Usually it's a guy reading the newspaper but not today. Is this clear? Are there any questions? OK.

As I said, you can work through this with Punnett Squares. I decided not to do it on the board because it takes a lot of time, but the book shows you, in this specific example, what you should expect. Here are the two parentals. They're homozygous for each of the alleles, big S, big S, big Y, big Y, little S, little S, little Y, little Y. In the F1 generation you create the double heterozygote, big S, little S, big Y, little Y, and then that generates the four gametes in equal proportion, as we just discussed.

If you cross two of these F1s together then you can create a Punnett Square which now has 16 squares instead of just four which allows us to consider the products of all four of these gametes crossed to all four of these gametes. So we get various combinations of genotypes and we get various combinations of phenotypes. And you can calculate what those are based on looking at this. There's actually another way of doing it, which I find to be simpler, which is illustrated here.

Again, because the traits and the alleles are segregating from one another independently you can think about this as two Punnett Squares separately and figure out the consequences of those two traits by simply multiplying between them. So what I mean by that is if you consider the S allele in isolation then there are the familiar 1:2:1 ratio of the three different genotypes.

And that's true also of the Y genotypes, 1:2:1 of the three possible genotypes. In total there are nine possible genotypes, but when you separate it from S and Y it's 3:3. Likewise with respect to the phenotypes, three-quarters of these guys will be smooth, one-quarter

will be wrinkled. And over here three-quarters will be yellow, one-quarter will be green. If I want to figure out what the frequency is of any compound genotype, I just have to multiply across.

So if I want to know the frequency of big S, big S, big Y, big Y, and it's just the product of a quarter times a quarter or a sixteenth, just like the coins example by the way. If I want to know the frequency of being big S, little S, big Y, little Y, then it's a half times a half or four-sixteenths, sorry. A half times a half or a quarter which equals four sixteenths.

And the other genotypes comprise the remaining sixteenths that we see, another 11. And likewise with respect to phenotypes. If you want to know the frequency of smooth yellow offspring you just multiple across, three-quarters times three-quarters gives you nine-sixteenth. Of wrinkled green ones it's a quarter times a quarter or one-sixteenth. So, again, when you're asked to do Punnett Squares for two traits that segregate independently, you might think about doing it using separate Punnett Squares.

OK. So we've talked about Mendel's Laws. We're wrapping up Mendel's Laws here. The first law is independent segregation of the two alleles. The second law with respect to different genes, they segregate independently from each other. OK?

Now, as I said, this is true for genes that are on different chromosomes or actually genes that are far away on the same chromosome, but it's not always true. And to emphasize that point we're going to return to our coin friends.

So let me just remind you, let me just remind you what we saw. So this doesn't apply to genes that are linked together on the same chromosome.

Let's remind you what we determined for genes that are unlinked, the dime and the penny. We said that the frequency of getting in my left hand head, head and in my right hand head, head, and together was 1:4 and 1:4 and together was 1:16. That was the situation when they were independent of one another. But let's consider the situation when I've taped them together. Now I have a penny and a quarter which are taped together.

I have fixed the orientation of these two coins with respect to one another. So you can see the heads are on the same side, the heads

are on the same side, yeah? OK. What's the likelihood that this is going to have the penny in the head configuration?  $1:2$ . And if it is what's the likelihood that the quarter is going to be in the head configuration?

One. So what's the likelihood that the coin is going to have head, head when I turned it up?  $1:2$ . Not like this example.  $1:2$ . And so what's the likelihood that it's going to be head, head in this configuration, in this hand?  $1:2$ . So what's the likelihood that it's going to be head, head, head, head?  $1:4$ . So the frequencies don't work out, according to Mendel's Rules, if the two genes are linked, the two genes are linked together.

So thank you for your help. It pays to sit in the front row every once in a while. So this is what we just talked about. In my left hand the frequency of head, head was one-half, in my right hand frequency of head, head was one-half, so the product was a half times a half or a quarter. OK? Now, if we want to think about that is sort of genetic terms, let's think about chromosomes.

And genes can be linked on chromosomes like those two coins can be linked together by tape. So here are two genes, the penny gene and the quarter gene, two alleles, the head allele and the tail allele, and they're present on two chromosomes in a heterozygous individual. And they're in this configuration such that the head allele of the quarter is next to the head allele of the penny. The tail allele of the quarter is next to the tail allele of the penny.

When this goes through meiosis the alleles stick together. The head alleles stick together in the gametes. The tail alleles stick together in the gametes. It's just like Mary Had a Little Lamb. Remember that one? I'm getting curious looks. Mary had a little lamb. Its fleece was white as snow. Everywhere that Mary went the lamb was sure to go. A long way to go for that one, but anyway.

Everywhere that Mary went the lamb was sure to go. They stay linked. OK? And importantly you don't find, or you almost never find this situation where the quarter in the head, sorry, the penny in the head configuration went with the quarter in the tail configuration. You don't find those, or you almost never, and this is the point of the final phase of the lecture. OK. Very good.

So let's look at this with respect to peas. Why not? We're going to talk about now linked genes in peas. We're going to talk about two genes.

We're going to have our familiar Y gene which has its two alleles. And now we're going to talk about a new gene, the D gene, which likewise has two alleles and two phenotypes which are dense peas and light peas. OK? Dense peas and light peas. And it turns out that these two genes are on the same chromosome and very close to one another.

So if you think about the chromosomes in a heterozygous individual, double heterozygous individual they would look like that. If we think about the chromosomes in a tester strain, which is homozygous for the recessive alleles for both.

What's going to happen to the offspring? What? What? I'm sorry. First of all, this phenotype is yellow and dense. Big D is dominant over little D. This phenotype is green and light.

OK? What do the gametes look like in this Punnett Square? And why am I drawing four boxes, only four boxes anyway? Didn't I tell you a little while ago that if you have two alleles, two genes you have to draw a Punnett Square with 16 boxes? Why am I drawing only four? Because they go together. They're linked. So what do the alleles look like?

Well, this parent is going to give either big Y, big D or little Y, little D. And this parent is always only ever going to give little Y, little D. OK? So therefore the genotype follows, sorry.

And the phenotype. What am I going to get when I deconvolute this? What am I going to get? The phenotype in that cross, 50% will be yellow dense. And 50% will be what? Green and light.

The very same two phenotypes that I got in the parents. These are the parental phenotypes.

And in a test cross like this, of two genes that are very tightly linked, you would always regenerate the parental phenotypes. They would never separate from one another. You'd always only ever generate the parental --